PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION See Form PCT/IPEA/416	
2021739PC/ko		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/FI2003/000875	17.11.2003	18.11.2002
International Patent Classification (IPC) or national classification and IPC		
G01N 33/94, G01N 33/53, C07K 16/42		
Applicant		
Valtion Teknillinen Tutkimuskeskus et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))
      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
21.05.2004	01.02.2005
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. +46 8 667 72 88	Authorized officer Malin Söderman/EÖ Telephone No. +46 8 782 25 00

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/FI2003/000875

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))
☐ publication of the international application (under Rule 12.4)
☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

☒ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ the claims:

pages _____ as originally filed/furnished
pages* _____ as amended (together with any statement) under Article 19
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ the drawings:

pages _____ as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☒ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-25	YES
	Claims		NO
Inventive step (IS)	Claims	1-25	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-25	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Reference is made to the following documents:

D1: US6326159 B1
D2: ULLMAN et al. Anti-immune complex antibodies enhance affinity and specificity of primary antibodies. Proc. Natl. Acad. Sci., 1993, Vol. 90
D3: ARAI et al. Fluorolabeling of antibody variable domains with green fluorescent protein variants: application to an energy transferbased homogeneous immunoassay. Protein Engineering, 2000, Vol. 13, no. 5
D4: JP 2001174460 A. Database WPI, 2001 (abstract)
D5: LITTLE et al. Generation of a large complex antibody library from multiple donors. Journal of Immunological Methods, 1999, Vol. 231
D6: CHARLTON et al. The isolation of super-sensitive anti-hapten antibodies from combinatorial antibody libraries derived from sheep. Biosensors & Bioelectronics, 2001, Vol. 16
D7: BOLGER et al. Preparation and characterization of antisera and monoclonal antibodies to haloperidol. Immunological Investigations, 1985, Vol. 14, no.6

The invention relates to a non-competitive immunoassay for small analytes, wherein the analyte is reacted with two binding partners. The first binding partner binds to the analyte to form a complex between the first binding partner and the analyte, and the second binding partner binds to the complex formed by the first binding partner and the analyte. The resulting complex is detected. The second binding partner is obtained from a display recombinant binding partner library.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box V

D1 relates to a method which comprises forming an immune sandwich complex comprising a monoepitopic antigen or an analog thereof, a first monoclonal antibody that binds to the monoepitopic antigen, a second monoclonal antibody that is an antibody of the invention, and measurement of the immune sandwich complex, see abstract. The non-competitive immunoassay described in the claimed invention according to claim 1 is considered to correspond to the immune sandwich complex immunoassay described in D1. According to D1, the analytes of interest will generally be compounds which have a molecular weight less than 1500 and include drugs like morphine, see D1. The small analyte described in claim 1 is considered to correspond to the analytes described in D1. D1 describes the use of homogeneous assays wherein an aqueous medium is used, see column 2, lines 57-65. The homogeneous assay described in claim 3 is considered to correspond to the homogeneous assay described in D1. Compositions of matter and kits for use in conducting an assay in accordance with the invention are also disclosed in D1.

D2 describes an antibody that recognizes an immune complex of an antibody to tetrahydrocannabinol (THC). The anti-IC antibody was obtained by using an affinity labelled anti-THC antibody as immunogen and selecting an anti-IC antibody, the binding of which was enhanced by the presence of A9THC.

D3 describes a homogeneous non-competitive immunoassay using FRET, see abstract.

D4 relates to an immunoassay for measuring hapten, e.g. estradiol, using labelled antibodies which are directed against an immune complex, comprising hapten and anti-hapten antibodies which are indirectly coupled to water-insoluble support, see abstract.

D5 describes generation of a large complex antibody library from multiple donors, see abstract.

D6 describes a method for finding antibodies from antibody libraries and using the antibodies in immunoassays, see abstract.

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box V

D7 describes preparation and characterisation of antisera and monoclonal antibodies to haloperidol, see abstract.

The cited documents represent the general state of the art.

The invention defined in claims 1-25 is not disclosed by any of these documents.

The cited prior art does not give any indication that would lead a person skilled in the art to the claimed invention that provides reagents suitable for a non-competitive immunoassay for small analytes where a display recombinant binding partner library is used to select a binding partner that selectively binds to the complex between the analyte and the primary antibody. Therefore, the claimed invention is not obvious to a person skilled in the art.

Accordingly, the invention defined in claims 1-25 is novel and is considered to involve an inventive step. The invention is industrially applicable.